UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,480	10/25/2000	James A. Spudich	18557A-00021	9741

7590 07/15/2003

MAHA A. HAMDAN
MEDLEN & CARROLL. LLP
101 HOWARD STREET,
SUITE350
SAN FRANCISCO., CA 94105

EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 07/15/2003 16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/486,480	Spudich et al.
Examiner	**Art Unit**
S. Devi, Ph.D.	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 8, 2003*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-13* is/~~are~~ pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☒ Claim(s) *13* is/~~are~~ allowed.

6) ☒ Claim(s) *1-12* is/~~are~~ rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of Reference Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 04/08/03 (paper no. 14) in response to the non-final Office Action mailed 12/13/02 (paper no. 12). With this, Applicants have amended the specification.

Status of Claims

2) Claims 14-55 have been canceled via the amendment filed 04/08/03.

Claims 1, 6, 7 and 13 have been amended via the amendment filed 04/08/03.

Claims 1-13 are pending and are under examination.

Objection(s) Withdrawn

3) The objection to the specification made in paragraph 9 of the Office Action mailed 12/13/02 (paper no. 12) is withdrawn in light of Applicants' amendment to the specification.

Prior Citation of Title 35 Sections

4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Withdrawn

6) The rejection of claim 6 made in paragraph 10(a) of the Office Action mailed 12/13/02 (paper no. 12) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

7) The rejection of claim 7 made in paragraph 10(b) of the Office Action mailed 12/13/02 (paper no. 12) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

8) The rejection of claims 1 and 4-12 made in paragraph 12 of the Office Action mailed 12/13/02 (paper no. 12) under 35 U.S.C. § 103(a) as being unpatentable over Hirabayshi *et al.* (*J. Mol. Recog.* 3: 204-207, 1990) (Hirabayashi *et al.*, 1990) in view of Mueller *et al.* (*Biophys. J.* 68:

1681-1686, 1995), is withdrawn.

9) The rejection of claims 1-12 made in paragraph 13 of the Office Action mailed 12/13/02 (paper no. 12) under 35 U.S.C. § 103(a) as being unpatentable over Hirabayshi *et al.* (*J. Chromatogr.* 597: 181-187, 1992 - Applicants' IDS) (Hirabayashi *et al.*, 1992) in view of Mueller *et al.* (*Biophys. J.* 68: 1681-1686, 1995), is withdrawn.

10) The rejection of claims 1-5, 8 and 9 made in paragraph 14 of the Office Action mailed 12/13/02 (paper no. 12) under 35 U.S.C. § 103(a) as being unpatentable over Mueller *et al.* (*Biophys. J.* 68: 1681-1686, 1995) in view of Hirabayshi *et al.* (*J. Chromatogr.* 597: 181-187, 1992 - Applicants' IDS) (Hirabayashi *et al.*, 1992), is withdrawn.

11) The rejection of claims 1-12 made in paragraph 15 of the Office Action mailed 12/13/02 (paper no. 12) under 35 U.S.C. § 103(a) as being unpatentable over Sassenfeld *et al.* (*Biotechnol.*2: 76-81, 1984) in view of Geke *et al.* (*J. Colloid and Interface Science* 189: 283-287, 15 May 1997- already of record), is withdrawn. Applicants are asked to note the new rejection made below.

Response to Applicants' Arguments on Relevant parts of Sassenfeld *et al.*

12) Applicants acknowledge that Sassenfeld *et al.* taught the production of human urogastrone with a C-terminal polyarginine by recombinant DNA technology and then purifying the peptide fusion by ion-exchange purification. Applicants contend that Sassenfeld's purification is a two step ion-exchange purification. Applicants state that the first step was based upon the unusual basicity of the polyarginine-fused protein and that the polyarginine was removed by carboxypeptidase B before the second step.

Applicants' arguments have been carefully considered, but are non-persuasive. First, the invention claimed in the instant claims is not limited to a 'one step-process'. The open claim language used in the claims includes, but does not exclude, any number of method steps. Instant claims are not drawn to a method of purification, but to a method of attaching a moiety to a surface of a layered silicate. Furthermore, Sassenfeld *et al.* indeed taught a single step purification procedure and concluded that the considerable purification was due to the unusual basicity of the polyarg-fused protein (see paragraph bridging left and right columns on page 78). A single-step purification is taught to be ideal, simpler, more efficient and has been recommended (see page 79, right column).

Rejection(s) under 35 U.S.C. § 103

13) Claims 1-12 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Sassenfeld *et al.* (*Biotechnol.*2: 76-81, 1984, already of record) in view of Suzuki *et al.* (4,629,713) and Pinnavaia *et al.* (US 5,993,769).

The reference of Pinnavaia *et al.* is applied in this rejection because it qualifies as prior art under subsection (e) of 35 U.S.C § 102 and accordingly is not disqualified under U.S.C 103(a).

The transitional phrases "comprising", "consisting essentially of" and "consisting of" define the scope of a claim with respect to what unrecited additional components or steps, if any, are excluded from the scope of the claim. The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. *Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948)* ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts").

Sassenfeld *et al.* taught a method of attaching, conjugating or fusing a recombinant protein biomolecule moiety, such as, human urogastrone having a C-terminal polyarginine (i.e., tag), for use in ion-exchange purification (see abstract). Sassenfeld's method included the loading of the polyarginine tagged-urogastrone extract onto the cation exchange resin substrate (see page 77, right column). That this loading step necessarily involves or includes contacting the arginine tag with the surface of the cation exchange resin is implicit from the teachings of Sassenfeld *et al.* Sassenfeld's method further comprised the elution (which involves contacting with the surface of the cation exchange resin to remove bound molecules) with 400 mM sodium salt (see page 77, right column, including the Figure 1 legend). The polyarginine is attached at the carboxyl terminus of the urogastrone and comprises about five arginine residues (see page 77, column bridging left and right columns). Sassenfeld's method involved the insertion of the synthetic DNA sequence coding for five additional arginines into the beta-urogastrone gene (see page 77, left column). That this insertion or fusion includes or results in covalent attachment between the encoded arginine tag and beta-urogastrone is implicit from the teachings of Sassenfeld *et al.*

Sassenfeld *et al.* do not teach the use of a layered silicate substrate or mica in their method. However, the layered silicates as alternate cation exchange substrates were well known in the

art at the time of the invention. For instance, in 1986, Suzuki *et al.* taught layered mica, montmorillonite, bentonite etc. as materials possessing abundant cation-exchange ability (see lines 12-32 in column 1).

Pinnavaia *et al.* taught layered silicates, such as, synthetic mica montmorillonite or muscovite mica and their highly preferred advantageous use as layered inorganic ion exchangers due to their low cost and the broad range of particle sizes (see first full paragraph in column 23).

Given the art-recognized abundant cation-exchange ability of layered silicates, such as, mica, or montmorillonite, as expressly taught by Suzuki *et al.*, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to replace Sassenfeld's cation exchange resin material with Suzuki's layered silicate cation-exchange material, such as, mica or montmorillonite, to produce the instant invention with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of cost effectiveness, since Pinnavaia *et al.* explicitly taught that layered inorganic ion exchangers are highly preferred due to their advantageous low cost and broad range of particle sizes. Substitution of one ion exchange material with another, alternative, cheaper, art-known ion exchange material would have been obvious to one of skill in the art, would have been well within the realm of routine experimentation and would have brought about similar results.

Claims 1-12 are *prima facie* obvious over the prior art of record.

Relevant Prior Art

14) The prior art made of record and not relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

- The use of polyarginine tails in ion chromatography was well known in the art at the time of the invention. Keeling *et al.* (US 6,107,060, filed 09/30/1996) taught that ion chromatography methods have been enhanced in the art with the use of polarginine tails which increase the overall basicity of the protein, thus enhancing binding to ion exchange column (see column 4, lines 15-19).

- Brewer *et al.* (US 4,880,911) disclosed a method of covalently attaching polyarginine to a polypeptide molecule and contacting the resultant molecule with ion exchange materials, such as, SM-Sepharose CL-6B or SP-Sepharose (see entire document).

The use of attaching a spacer to the surface of silica was well known in the art at the time of the invention. Konnecke *et al.* (*Monatschefte fur Chemie* 113: 331-337,1982) taught the use of silica supports for coupling biomolecules via covalent bonds (see page 331). Silica gel is taught to be relatively stable to treatment with common organic solvents and in aqueous solution and that it does not swell. Konnecke *et al.* taught the need for a sufficiently long spacer for coupling to prevent steric interactions between the biomolecule enzyme protein and the silica surface (see page 335). Silica is described as a porous material with cavities of different sizes. It is taught that during the chemical modification of the silica, groups are anchored in smaller pores and cavities being inaccessible to the large high molecular weight enzymes despite the use of the large spacer (see page 335).

The following prior art references taught the conventional nature and the routine use of layered silica or mica as an alternative substrate for attaching a biomolecule moiety, or in ion exchange:

- Sugimori *et al.* (JP 356152741), in 1981, taught the ion exchangeability of the laminated silicate, such as, montmorrillonite and vermiculite (see abstract).
- Charych (US 6,468,759) taught mica, silica gel beads, Sepharose and Sephadex as alternative solid supports for immobilization of biopolymers (see column 34, lines 38-46; column 3, lines 44-50; and claims 13, 12 and 1).
- Xu *et al.* (US 5,874,668) taught mica to be a negatively charged substrate (see column 17, lines 14-40).
- Lloyd *et al.* (US 5,177,005) taught covalent linking and adsorption immobilization of biomolecules on supports, such as, bentonite, ion exchange resins, kalinite, Sephadex, silica gel (see column 1, lines 38-64).
- Kusakabe *et al.* (US 4,614,714) taught Sephadex, polyamino acid, silicone resins, ion-exchange resins and bentonite as suitable carriers or supports for immobilization of biomolecules (see column 15).
- Elahi (US 4,338,094) taught the use of physical adsorbents, such as, bentonite particles to which antibody molecules can be linked (see second full paragraph).
- Gaafar (US 4,029,756) taught silica, bentonite, Sephadex and Sepharose as alternate

particulate carriers or substrates on which biomolecules are conjugated or adsorbed (see paragraph bridging columns 7 and 8).

- Brizzard *et al.* (US 6,379,903) described Sassenfeld's work as follows (see column 1, lines 27-35):

> One method used to purify hybrid polypeptides is the polyarginine system in which a hybrid polypeptide is selectively purified on a cation exchange resin. See Sassenfeld, H.M. and Brewers, S.J. *BioTechnology* 2: 76 (1984); U.S. Pat. No. 4,532,207. Sassenfeld and Brewer reported a carboxy-terminal extension of five arginine residues fused to a target protein. This basic polyarginine extension allowed the purification of the hybrid polypeptide on a SP-Sephadex resin.

- Dorval *et al.* (US 5,561,045) taught an exemplary list of supports useful for hydrophobic coupling to antibodies, included in which are silica, silica gels and bentonite (see column 6, lines 36-47).

- Neurath *et al.* (US 5,230,998) taught various water-insoluble supports, such as, silica, kaolinite, silica gel, bentonite, Sephadex and hydroxyapatite, for physical adsorption (see column 11, lines 43-57).

- Suzuki *et al.* (US 4,629,713) taught mica, bentonite and montmorillonite to be smectite type materials having abundant cation-exchange ability (see column 1, lines 12-32).

Remarks

15) Claims 1-12 stand rejected. Claim 13 is allowed.

16) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which is able to receive transmissions 24 hours a day and 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

17) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the

Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

June, 2003

S. DEVI, PH.D.
PRIMARY EXAMINER